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2002952117 10 October 2002 (10.10.2002) AU(71) Applicant (for all designated States except US): **FUJISAWA PHARMACEUTICAL CO., LTD.** [JP/JP]; 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP).

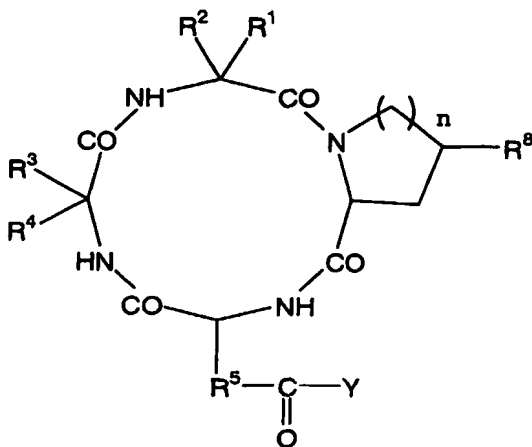
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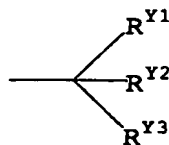
[Continued on next page]

(54) Title: CYCLIC TETRAPEPTIDE COMPOUND AND USE THEREOF

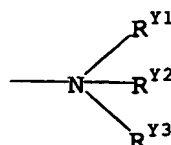


(I)

(57) Abstract: A cyclic tetrapeptide compound of the formula (I): wherein  $R_1$  is hydrogen;  $R_2$  is lower alkyl, aryl, optionally substituted ar(lower)alkyl, heterocyclic(lower)alkyl, cyclo(lower)alkyl(lower)alkyl, lower alkylcarbonyl(lower)alkyl or arylcarbonyl(lower)alkyl;  $R_3$  and  $R_4$  are each independently hydrogen, lower alkyl, optionally substituted ar(lower)alkyl, optionally substituted heterocyclic(lower)alkyl or cyclo(lower)alkyl(lower)alkyl, or  $R_3$  and  $R_4$  are linked together to form lower alkylene or condensed ring, or one of  $R_3$  and  $R_4$  is linked to the adjacent nitrogen atom to form a ring;  $R_5$  is lower alkylene or lower alkenylene, Y is [wherein  $R_{Y1}$  is hydrogen, halogen or optionally protected hydroxy,  $R_{Y2}$  is hydrogen, halogen, lower alkyl or phenyl, and  $R_{Y3}$  is hydrogen or lower alkyl];  $R_8$  is hydrogen or lower alkyl; and n is an integer of 1 or 2, or a salt thereof.



(II)



(III)



CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 02/13754

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K5/12 A61K38/12 A61P29/00 A61P35/00 A61P37/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 21979 A (HINO MOTOHIRO ;MORI HIROAKI (JP); FUJISAWA PHARMACEUTICAL CO (JP);) 20 April 2000 (2000-04-20) p. 1, l. 25; p. 2, l. 10-13; p. 7, l. 25, 28; p. 24, l. 25-p. 29, l. 7 ---	1-11, 13-22
X	WO 00 08048 A (ABE FUMIE ;HINO MOTOHIRO (JP); MORI HIROAKI (JP); YOSHIMURA SEIJI) 17 February 2000 (2000-02-17) page 1, line 33,34 page 6, line 10-15 ---	1-11, 13-22
X	EP 1 010 705 A (JAPAN ENERGY CORP) 21 June 2000 (2000-06-21) p. 3, l. 27-29 & compounds X-XXI; XXIII-XXXXIII --- -/--	1-11, 13-22

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 99/13754

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 07042 A (COLLETTI STEVEN L ;WYVRATT MATTHEW J (US); GURNETT ANNE M (US); ME) 1 February 2001 (2001-02-01) p. 1, l. 7-9 & examples 4a; 20b; 21b; 22b; 23b; 27; 29; 30; 32; 33; 52b; 53; 55a; 68-100; 102-110; 120-125; 127-132; 145-147; 152-157; 163; 164; 169; 170 -----	1-11, 13-22
X	GB 2 309 696 A (MERCK & CO INC) 6 August 1997 (1997-08-06) p. 2, l. 30-31 & p.6, l. 5-p. 7, l. 7. -----	1-11, 13-22

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/JP 02/13754

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 12 and 23  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1, 4-11 (partially); 2, 3, 13-22 (completely)

Compounds of formula I, wherein  $n=1$  and Y is  $-C(RY1)(RY2)(RY3)$ , their compositions and use

2. Claims: 1, 4-11 (partially); 2, 3 (completely)

Compounds of formula I, wherein  $n=2$  and Y is  $-C(RY1)(RY2)(RY3)$ , their compositions and use

3. Claims: 1, 4-11 (partially)

Compounds of formula I, wherein  $n=1$ ,  $R8=H$  and Y is  $-N(RY1)(RY2)(RY3)$ , their compositions and use

4. Claims: 1, 4-11 (partially)

Compounds of formula I, wherein  $n=2$ ,  $R8=H$  and Y is  $-N(RY1)(RY2)(RY3)$ , their compositions and use

5. Claims: 1, 4-11 (partially)

Compounds of formula I, wherein  $n=1$  or  $2$ , Y is  $-N(RY1)(RY2)(RY3)$  and  $R8$  is different from H, their compositions and use

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Continuation of Box I.1

Although claims 7, 10, 18 and 21 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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Continuation of Box I.1

Claims Nos.: 12 and 23

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy  
Rule 39.1(v) PCT - Presentation of information

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 02/13754

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